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Cutaneous Metastases From Prostatic Carcinoma

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Cutaneous metastasis from carcinoma of the prostate is a rare phenomenon. When it occurs, metastases usually appear as multiple nodules involving the suprapubic area and the anterior aspect of the thighs. We report on two cases of cutaneous metastases from prostatic carcinoma, one of them presenting the stereotypical clinical and histopathological findings, whereas in the other one cutaneous metastasis consisted of a morphea-like plaque on the chest. Histopathologically, the later case revealed accumulations of neoplastic cells distributed in a folliculotropic pattern. In both examples immunohistochemical study with prostatic specific antigen (PSA) confirmed the prostatic origin of the metastases. We review the literature on this subject.

KEY WORDS: **prostatic specific antigen, folliculotropic metastasis, prostate carcinoma**

INTRODUCTION

Prostatic carcinoma is the most frequent malignancy in males [1]. The most common sites of metastases are bones, lungs, liver, and adrenal glands. Cutaneous metastases from prostatic carcinoma, however, are rare. We report on two cases of this condition and demonstrate that immunohistochemical study with prostate specific antigen (PSA) is helpful to prove the prostatic origin of the lesions. One of our cases showed the stereotypical clinico-pathological findings, whereas the second one presented an unusual clinical manifestation, characterized by a large morphea-like plaque on the anterior aspect of the chest, and the histopathologic study revealed accumulations of neoplastic cells in a folliculotropic arrangement.

Case 1

A 64-year-old white male developed bone metastases 2 years after the initial diagnosis of prostatic carcinoma. Skeletal survey showed involvement of 12 dorsal vertebra, some ribs, and the skull. In spite of goserelin and flutamide therapy, a mononeuritis of VI craneal nerve secondary to skull involvement and, axillary and supraclavicular lymphadenopathy appeared 1 year later. Subsequently, therapy with estramustine and vinblastine was tried unsuccessfully. Serum levels of PSA and prostatic acid phosphatase had been elevated from the first diagnosis of the disease.

Finally, in May 1994 the patient was submitted to our department to assess cutaneous lesions. Physical examination disclosed an indurated erythematous plaque involving the chest, with sharp and irregular borders. Within this plaque, alopecia was evident and some papular lesions were observed. A biopsy was performed.

Histopathologic study demonstrated accumulations of neoplastic cells involving and destroying hair follicles (Fig. 1) and some erector pili muscle fibers. Although almost all hair follicles included in the cutaneous biopsy were involved and altered by neoplastic cells, other cutaneous adnexa were spared. In addition to these findings, the stereotypical findings of cutaneous, metastatic strands and cords of neoplastic undifferentiated cells between normal collagen bundles were present. Neoplastic cells showed atypical nuclei containing one or more conspicuous eosinophilic nucleoli (Fig. 2). Atypical mitotic figures were seen in some fields.

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Fig. 1. Case 1. Hair follicle destroyed by neoplastic cells. The erector pili muscle is preserved.

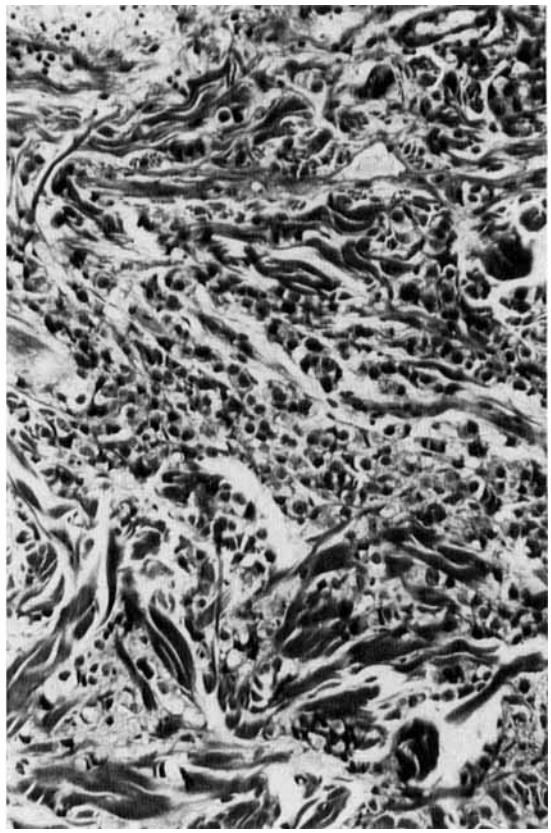

Fig. 2. Case 1. High magnification showing neoplastic cells with a large round nuclei containing one or more conspicuous eosinophilic nucleoli.

Immunohistochemical studies demonstrated CAM 5.2 anti-human cytokeratins 8 and 18 (Becton Dickinson, San Jose, CA) K and PSA positivity. Chromogranin immunostaining was negative. When cutaneous metastasis was diagnosed, alpha-interferon, 5-fluorouracil, and cisplatin therapy was instituted, but the patient died 6 weeks later.

Case 2

A 67-year-old caucasian male was diagnosed with prostatic carcinoma in April 1993. Two months later, bone metastases were disclosed by radionuclide imaging. Subsequently, in April 1994 the patient was admitted to the hospital because of rectal bleeding. A colonoscopy failed to demonstrate extension to the colon of the prostatic disease. At that time, an abdominal ultrasound scan showed a hepatic nodule, which was interpreted as a metastatic lesion, although no further studies were carried out. Finally, in June 1994 the patient presented with 20 cutaneous firm nodules measuring less than 1.5 cm in diameter distributed through the abdominal area. A biopsy of one of them was performed.

Histopathologic study disclosed two large accumulations of crowded neoplastic cells located in the reticular dermis. Moreover, strands of epithelial undifferentiated neoplastic cells intermingled with normal collagen bundles were present at the periphery of the large masses, involving the full thickness of the dermis and the subcutaneous fat (Fig. 3). Neoplastic cells showed round atypical nuclei with prominent eosinophilic nucleoli, and scant and clear cytoplasm. A relative nuclear monomorphism was detected. Few mitotic figures were disclosed through the aggregations of neoplastic cells.

Immunohistochemical study demonstrate prostatic specific antigen (PSA) and CAM 5.2 cytokeratin positivity. Chromogranin immunostaining marked 25–50% of the neoplastic cells. The serum level of PSA ranged from 1.5 ng/ml during hormonal therapy to 451.8 ng/ml before this therapy. At the present time, 6 months after the onset of cutaneous metastases, the patient is still alive.

DISCUSSION

Carcinoma of the prostate is the most common malignancy in males [1]. It may be underdiagnosed because Harbitz and Haugen [2] found prostatic carcinoma in 50% of autopsies of unselected males over 70 years old. Nevertheless, in spite of the high incidence of carcinoma of prostate, cutaneous metastases from it are rare. In a series of 724 cutaneous metastases, Brownstein and Hel-

Fig. 3. Case 2. A nodule (bottom left) and strands and cords of neoplastic undifferenciated cells intermingled with normal collagen bundles.

wig [3] found a prostatic origin in only 1% of males, and Gates [4], in an autopsy series from patients with internal carcinoma including 2,298 cases, found only one example of cutaneous metastasis from prostatic adenocarcinoma. On the other hand, Held and Johnson [5] found an incidence of 0.3% of cutaneous metastases in a series of 961 patients with prostatic carcinoma. Other series, however, reported higher percentages of prostatic origin in cutaneous metastases, namely, Chimenti [6] found an incidence of 5.8% and Reingold [7] reported an incidence of 9.2%.

Most authors [8,9] classify cutaneous metastases into three different clinical patterns: (1) nodular, (2) inflammatory or erysipeloid, and (3) *en Cuirasse* or sclerodermoid. Actually, there is no correlation between any primary tumor and the cutaneous metastatic pattern, although some malignancies are more frequently related to a specific type of cutaneous metastasis; for example, hypernephroma usually presents as a single nodule with a vascular appearance. We found in our literature review that all clinical variants of cutaneous metastases, except the sclerodermoid type, have been described in prostatic carcinoma [6,10–17]. The most common clinical pattern of skin metastasis from carcinoma of the prostate is that of multiple nodules involving the suprapubic area and the anterior aspect of the thighs [14,18,19]. Our case 2 expressed this pattern, whereas case 1 showed an unusual clinical manifestation, characterized by a sclerodermoid plaque located on the chest.

Most authors believe that cutaneous metastases appear late in the disease and that they are a sign of poor prognosis. However, Marquis and Benson [18] stated that "skin metastases *per se* are not indicative of a poor prognosis," illustrated by the long-term survival of their patient, who presented with cutaneous metastases without other internal metastases. In some cases, skin metastasis was the first manifestation of prostatic carcinoma [17,20]. Both of our patients presented internal metastases before the development of skin involvement. Nevertheless, our case 2 is alive 6 months after the diagnosis of the cutaneous metastases.

Histopathological findings of cutaneous metastases from prostatic carcinoma are poorly described. Usually, glandular structures are present within the dermis in cutaneous metastases from prostatic carcinoma [10,12,19], although these were not found in any of our patients, probably because these cases consisted of undifferentiated carcinomas. Architecturally, skin involvement from prostatic carcinoma is similar to that of other malignancies, showing either nodules of neoplastic cells or strands of cells diffusely distributed between the collagen bundles.

Our first case showed an exceptional folliculotropic pattern. This histopathologic pattern was first described by Aguilar et al. [21] in a nodular metastasis on the vertex of a patient with squamous cell carcinoma of the larynx. In the case of the present report, histopathological findings may represent a previous step of sclerodermoid metastases where there is a diffuse distribution of the neoplastic cells in a dermis without hair follicles. The cytology of the cutaneous metastases from cancer of the prostate is rather characteristic, with cells showing round nuclei and one or more conspicuous eosinophilic nucleoli [10,12,19]. Our cases showed these cytologic aspects.

Serum levels of PSA, as well as prostatic acid phosphatase, are helpful in the follow-up of patients with prostatic carcinoma, although our second case showed no elevations of serum levels of PSA in correlation with the metastases. These two serum markers can be also investigated by peroxidase-antiperoxidase techniques in biopsy specimens to demonstrate, if positive, the prostatic origin of a metastasis [22,23], because immunohistochemical study of PSA and prostatic acid phosphatase have a specificity of 100% and also a high sensitivity [22,24], and only some undifferentiated prostatic tumors show negative results. Supporting this fact, our two cases showed positive immunostaining with PSA, which confirmed the prostatic origin of the metastases. Thus, in males faced with metastases of an adenocarcinoma of unknown origin, it is mandatory to perform an immunohistochemical study with PAS and/or prostatic acid phosphatase.

Positivity of immunohistochemical studies for chro-

mogranin indicates neuroendocrine differentiation. Di Sant'Agenese [25], in his review, found 264 cases of prostatic carcinoma with some type of neuroendocrine differentiation and suggested that wide neuroendocrine differentiation may explain the resistance of some tumors to hormonal therapy.

In short, we have reported two examples of cutaneous metastases from prostatic carcinoma in which the primary malignancy could be established by immunohistochemical investigations for PSA.

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